What is the effect of dietary PUFA intake on health and intermediate health outcomes?

Conclusion

Strong and consistent evidence indicates that dietary n-6 polyunsaturated fatty acids (PUFA) are associated with improved blood lipids related to cardiovascular disease (CVD), in particular when PUFA is a replacement for dietary saturated fatty acids (SFA) or trans fatty acids. Evidence shows that energy replacement of SFA with PUFA decreases total cholesterol, LDL cholesterol and triglycerides, as well as numerous markers of inflammation. Polunsaturated fatty acid intake significantly decreases risk of CVD and has also been shown to decrease the risk of type 2 diabetes.

Grade: Strong

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades, click here.

Executive Summary Overview

Ten studies published since 2004 were reviewed to determine the effect of polyunsaturated fatty acids (PUFA) on health outcomes. These studies were conducted in the US, Canada, Europe and Australia. These included one methodologically strong pooled analysis of 11 prospective cohort studies (Jakobsen, 2009); five randomized controlled trials (RCTs), including two methodologically strong studies (Thijssen and Mensink, 2005; Thijssen, 2005) and three methodologically neutral studies (Liou, 2007; St-Onge, 2007; Zhao, 2004) ranging in size from 23 to 45 subjects; and four prospective cohort studies ranging in size from 1,551 to 78,778 subjects. Of these cohort studies, three were methodologically strong (Laaksonen, 2005; Mozaffarian, 2005; Oh, 2005) and one was methodologically neutral (Hodge, 2007). Randomized controlled trials that investigated the effects on serum lipid and lipoprotein levels of replacing saturated fat (SFA) with PUFA showed that PUFA improved serum lipid profiles (St. Onge, 2007; Zhao, 2004). Zhao et al (2004) found that high linoleic acid (LA) or high alpha-linolenic acid (ALA) diets, compared to the average American diet (AAD), decreased serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG) similarly. St-Onge et al (2007) reported that replacing snacks high in SFA or trans fats (TFA) with snacks high in PUFA, reduced LDL-C concentrations, TC and TG. However, varying LA, with SFA held constant, showed that high or low LA did not influence TC, LDL-C or high-density lipoprotein cholesterol (HDL-C) levels (Liou, 2007). Comparing individual fatty acids, diets providing 7% of energy from LA, stearic acid or oleic acid showed no significant (NS) differences in serum LDL-C or HDL-C (Thijssen and Mensink, 2005).

Randomized controlled trials that investigated the effects on serum lipid and lipoprotein levels of replacing SFA with PUFA showed that PUFA improved serum lipid profiles (St. Onge, 2007; Zhao, 2004). Zhao et al (2004) found that high LA or high ALA diets compared to the AAD decreased serum TC, LDL-C and TG similarly. St-Onge et al (2007) reported that replacing snacks high in SFA or TFA with snacks high in PUFA reduced LDL-C concentrations, TC and TG. However, varying LA, with SFA held constant, showed that high or low LA did not influence TC, LDL-C or HDL-C levels (Liou, 2007). Comparing individual fatty acids, diets providing 7% of energy from linoleic acid, stearic acid or oleic acid showed no significant (NS) differences in serum LDL-C or HDL-C (Thijssen and Mensink, 2005).

Studies that examined markers of inflammation or measures of oxidative stress showed PUFA improved inflammatory marker levels. Zhao et al (2004) reported that while both high ALA and LA diets decreased C-reactive protein (CRP), the finding was significant only for ALA. Additionally, while both high-PUFA diets similarly decreased intercellular cell adhesion molecule-1 (ICAM-1) vs. the AAD, the ALA diet decreased vascular cell adhesion molecule-1 (VCAM-1) and E-selectin more than the LA diet. The comparison of high vs. low LA, with SFA constant, showed no difference in CRP, interleukin-6 or platelet aggregation (Liou, 2007). Comparison of LA, stearic acid or oleic acid showed that, in men, platelet aggregation time was favorably prolonged with consumption of LA vs. stearic acid, but was not different compared to oleic acid (Thijssen, 2005).

Four prospective cohort studies showed that higher PUFA intake was associated with lower risk of coronary heart disease (CHD) and total mortality (Hodge, 2007; Laaksonen, 2005; Mozaffarian, 2005; Oh, 2005). A pooled analysis of 11 prospective cohort studies showed that risk of coronary events and coronary death was lowest with 5% energy substitution of SFA with PUFA>MUFA>carbohydrate (CHO) (Jakobsen, 2009).

The Nutrition Evidence Library (NEL) review for this question included a prospective study with nested case-cohort analyses on the effects of a dietary PUFA on type 2 diabetes (T2D) risk. The authors reported an inverse association between dietary LA and T2D, compared to a positive association for stearic acid and total SFA (Hodge, 2007). In addition, the review for this question is supplemented by evidence from question one on SFA and T2D risk that reviewed the literature from 2000. This, and the fact that blood lipids are intermediate markers of risk for both CVD and T2D, further supports the association between PUFA intake and decreased T2D risk.

Evidence Summary Paragraphs

Hodge et al, 2007 (neutral quality) This was a prospective study with nested case-cohort analyses conducted in Australia. The study investigated the associations of fatty acids in plasma and diet with diabetes incidence in the "Melbourne Collaborative Cohort" study of 3,737 adults aged 36 to 72 years old. Fatty acid intake and percent plasma phospholipid fatty acids (PL-FA) were measured at baseline, and diabetes incidence was assessed by self-report four years later. Logistic regression excluding (model 1) and including (model 2)body mass index (BMI) and waist-hip ratio (WHR) was used to calculate odds ratios (ORs) for plasma PL and dietary fatty acids. A positive association was seen for plasma phospholipid and diabetes for stearic acid [OR model 1, highest vs. lowest quintile: 4.14 (95% CI: 2.65, 6.49), P<0.0001] and total SFA [OR model 1: 3.76 (2.43, 5.81), P<0.0001], whereas an inverse association was seen for LA [OR model 1: 0.22 (0.14, 0.36), P<0.0001]. Dietary LA [OR model 1: 1.77 (1.19, 2.64), P=0.002], palmitic [OR model 1: 1.65 (1.12, 2.43), P=0.012], and stearic [OR model 1: 1.46 (1.00, 2.14), P=0.030] acids were positively associated with diabetes incidence before adjustment for body size. Within each quintile of LA intake, cases had lower baseline plasma phospholipid LA proportions than did controls. Authors concluded that dietary SFA intake is inversely associated with diabetes risk.

Jakobsen et al, 2009 (positive quality) This pooled analysis evaluated the associations between energy intake from MUFA, PUFA and CHO replacing energy from SFA to prevent CHD. Data from 11 American and European cohort studies involving 344,696 persons were pooled and analyzed for incident of CHD as outcome measures. During four- to 10-year follow-ups, there were 5,249 coronary events and 2,155 coronary deaths. The analysis found that for every 5% lower energy intake from SFAs and a concomitant higher energy intake from PUFAs or CHO, there was a significant inverse association between these energy sources and risk of coronary events, with hazard ratios (HR) as follows for PUFAs: HR, 0.87 (95% CI: 0.77, 0.97); HR for coronary deaths = +0.74 (95% CI: 0.61, 0.89), and for CHO: HR, 1.07 (95% CI: 1.01, 1.14); HR for coronary deaths = 0.96 (95% CI: 0.82, 1.13). Monounsaturated fat intake was not associated with CHD, nor was there modification by sex or age. The authors conclude that replacing SFAs with PUFAs rather than MUFAs or CHO prevents CHD over a wide range of intakes. The country and demographics of subjects not described.

Laaksonen et al, 2005 (positive quality) This was a prospective cohort study conducted in Finland. The study assessed the association of dietary LA and total PUFA intake with CVD and overall mortality in the Kuopio Ischemic Heart Disease Risk Factor (KIHD) Study,a random age-stratified sample (42, 48, 54 or 60 years old at baseline) of 2,682 men living in eastern Finland baseline between 1984 and 1989. One thousand five hundred fifty one middle-aged men participated in this study. Dietary fat composition was estimated with a four-day food record and serum fatty acid composition. During the 15-year follow-up, 78 men died of CVD and 225 of any cause. Total fat intake was not related to CVD or overall mortality. Men with an energy-adjusted dietary intake of LA [relative risk(RR) 0.39; 95% confidence interval (CI), 0.21 to 0.71] and PUFA (RR, 0.38; 95% CI: 0.20 to 0.70) in the upper third were less likely to die of CVD than men with intake in the lower third after adjustment for age. Multivariate adjustment weakened the association somewhat. Mortality from CVD was also lower for men with proportions of serum esterified LA (RR, 0.42; 95% CI: 0.21 to 0.80) and PUFA (RR, 0.25; 95% CI: 0.12 to 0.50) in the upper vs. lower third, with some attenuation in multivariate analyses. Serum and to a lesser extent dietary LA and PUFA were also inversely associated with overall mortality. Authors concluded that dietary fat quality may be more important than fat quantity in the reduction of cardiovascular mortality in men, dietary PUFA and more specifically LA intake may have a substantial cardio-protective benefit that is also reflected in overall mortality.

Liou et al, 2007 (neutral quality) The study was a randomized crossover feeding trial conducted in Canada. During the intervention, energy intake of ALA was a constant 1% of total energy, while LA intake was modified with low or high LA vegetable oils and fats to achieve an LA:ALA ratio of 4:1 or 10:1. 24 healthy subjects enrolled, mean age 27.9±1.1 years and 22 completed the study. Subjects consumed either a high-LA diet (10.5±0.53% of energy as LA, 1.1±0.06% as ALA) or low-LA diet (3.8 ± 0.12% of energy as LA, 1.0±0.05% as ALA) for four weeks each, without a washout period between diets. Prepared foods were provided to subjects. Dietary intakes were estimated using three 24-hour food records, kept at least four days apart, during the two four-week study periods. During the high-LA intake period, plasma phospholipids-LA levels were higher and eicosapentaenoic acid (EPA) levels were lower than during the low-LA intake period (P<0.001). Docosapentaenoic acid (DPA) levels declined over the eight-week period (P<0.001). Linoleic acid was inversely associated with EPA (R=-0.729, P<0.001), but positively associated with ALA:EPA ratio (R=0.432, P<0.001). Linoleic acid intake did not have any influence on ALA, arachidonic acid, DPA, docosahexaenoic acid (DHA) or TC, LDL-C or HDL-C, CRP or interleukin-6 or platelet aggregation.

Mozaffarian et al, 2005 (positive quality) This was a prospective cohort study conducted in the US. The researchers investigated the association between intermediate and long-chain n-3 PUFA and n-6 PUFA intake on the incidence of CHD in participants of the Health Professionals Follow-up Study. Dietary intake was assessed through FFQ administered at baseline and every four years, over 14 years of follow-up. 45,722 male health professionals (aged 40 to 75 years), free of known CVD at baseline, were included in the analysis. Over 14 years of follow-up, 218 sudden deaths, 1,521 non-fatal myocardial infarctions (MIs) and 2,306 total CHD events (combined sudden death, other CHD death and non-fatal MI) were identified. In multivariate-adjusted analyses, both long-chain and intermediate-chain n-3 PUFA intakes were associated with lower CHD risk, without modification by n-6 PUFA intake; intermediate-chain n-3 PUFAs were associated with CHD risk when n-3 PUFA intake was very low. In men with n-3 PUFA intake less than 100mg per day, each 1g per day of intermediate-chain n-3 PUFA intake was associated with an approximately 50% lower risk of nonfatal MI (HR=0.42, 95% CI: 0.23 to 0.75) and total CHD (HR=0.53, 95% CI: 0.34 to 0.83). Omega-6 PUFA intake was 7.6, 11.2 and 15.9g per day. Each 5g per day n-6 PUFA intake was NS associated with the risk of sudden death (HR=0.82; 95% CI: 0.63 to 1.06), non-fatal MI (HR=1.00; 95% CI: 0.91 to 1.11), or total CHD (HR: -0.96; 95% CI:

0.89 to 1.04).

Oh et al, 2005 (positive quality) This was a prospective cohort study (part of the Nurses' Health Study) conducted in the US. In this study the associations between dietary fat and specific types of fat with risk of CHD was examined among 78,778 US women (aged 30 to 55 years) initially free of CVD and diabetes in 1980. One thousand seven hundred sixty six incident CHD cases (including 1,241 non-fatal MI and 525 CHD deaths) were documented during 20 years of follow-up. From 1980 to 1998, the average intake of total fat decreased from 39.0% to 29.0%, SFA intake decreased from 15.65% to 9.4%, MUFA intake decreased from 16.0% to 11.5% and TFA intake decreased from 2.2% to 1.6%. Polyunsaturated fatty acid intake increased from 5.3% to 5.6%. Polyunsaturated fat intake was inversely associated with CHD risk (multivariate RR for the highest vs. the lowest quintile = 0.75, 95% CI: 0.60, 0.92; P=0.004). Trans-fat intake was associated with an elevated risk of CHD (RR = 1.33, 95% CI: 1.07, 1.66; P=0.01). A similar inverse association was observed between LA intake and risk of CHD; the relative risks for LA were one (referent), 1.02, 0.91, 0.87 and 0.77 (95% CI: 0.62, 0.95); P=0.01. The associations between intakes of PUFA and TFA with CHD risk were most evident among women younger than age 65 years (for PUFA, RR=0.66, 95% CI: 0.50, 0.85; P=0.002; for TFA, RR=1.50, 95% CI: 1.13, 2.00; P=0.01). The inverse association between PUFA intake and CHD risk was strongest among women whose BMI was 25 kg/m^2 or more. (Note: This study was included in the meta-analysis by Jakobsen et al, 2009).

St. Onge et al 2007 (neutral quality) This was a randomized crossover trial conducted in the US to determine whether replacing low-fat and high-fat or high-SFA and high-TFA fat snack foods with snacks foods high in PUFA and low in SFA and TFA improves CVD risk factors. The trial consisted of three 25-day controlled feeding periods with snacks, separated by a four- or eight-week washout period, over a period of seven months. Forty-five subjects were enrolled and 33 (seven male, 26 female, mean age 41.8±1.9 years) subjects completed all three phases. Subjects followed the same base diet except for the types of snacks included, either low-fat (30.8% of energy from fat, 5.2% of energy from PUFAs), high-PUFA (36.3% of energy from fat, 9.7% of energy from PUFAs), or high-fat (37.9% of energy from fat, 5.8% of energy from PUFAs). All food was provided to the subjects. All three diets reduced LDL-C and TC concentrations. LDL cholesterol decreased by 11.8% on low-fat, 12.5% on high-PUFA, compared with 8.8% on high-fat (P=0.03 and P=0.01, respectively), and TC decreased by 10.5% on low-fat, 10.7% on high-PUFA, compared with 7.9% on high fat (P=0.03 and P=0.02, respectively). There were NS effects of the diets on WC, percentage body fat or BP.

Thijssen et al, 2005; Thijssen and Mensink, 2005 (positive quality) This was a randomized multiple crossover study conducted in the Netherlands. The study compared the effects of stearic, oleic and LA on platelet aggregation, coagulation, fibrinolysis and hematological variables in 45 healthy subjects (18 men and 27 women, mean age 51 years, range 28 to 66 years). Subjects consumed three test diets in random order over three five-week periods, and after each intervention period, there was a washout period of at least one week when participants consumed their habitual diets. The test diets contained approximately 35% of energy from fat, and each diet contained 7% of energy as LA, stearic acid or oleic acid. Subjects visited a dietitian at least once every week to receive a new supply of products and to be weighed. Individual allowances were adjusted when subjects' weight differed by 1.5kg from the initial weight during week one or 2kg during the following weeks. The authors found that in men, ex vivo platelet aggregation time as measured by filtragometry (P=0.036 for diet effects) was favorably prolonged during consumption of the PUFA diet compared with the stearic acid diet (P=0.040). No effect was found in women after the high LA diet. The number of erythrocytes was lower and the mean platelet volume of the subjects decreased during consumption of the stearic acid diet by 0.32fL compared with the oleic acid diet (P<0.001) and by 0.35fL compared with the linoleic acid diet (P<0.001). The effects on coagulation and fibrinolytic variables did not differ among the other two fatty acids. Thijssen and Mensink, 2005, found no significant differences in serum LDL-C (P=0.137 for diet effects) or HDL-C (P=0.866). Very-low-density lipoprotein (VLDL) particle sizes and lipoprotein subclass distributions also did not differ significantly between the three diets.

Zhao et al, 2004 (neutral quality) This was a randomized controlled, three-diet, three-period, crossover study conducted in the US. The study evaluated the effects of ALA diet, LA diet compared to the AAD on multiple cardiovascular disease risk factors. Twenty-three hypercholesterolemic subjects (20 males, three females, mean age 49±1.6 years) enrolled and completed the trial. Subjects consumed three diets for six weeks each, separated by a washout period of less than three weeks. The ALA Diet provided 17% energy from PUFA (10.5% LA; 6.5% ALA); the LA Diet provided 16.4% energy from PUFA (12.6% LA; 3.6% ALA); and the AAD provided 8.7% energy from PUFA (7.7% LA; 0.8% ALA). Each diet period was six week with a three-week or less break between diet periods to improve diet compliance. Both high-PUFA diets, including the LA diet, decreased serum TC, LDL-C and TG similarly (P<0.05). The ALA Diet decreased CRP (CRP, P=0.01), whereas the LA Diet tended to decrease CRP (P=0.08). Both high-PUFA diets similarly decreased intercellular cell adhesion molecule-1 vs. AAD (-19.1% by the ALA Diet, P<0.01; -11.0% by the LA Diet, P<0.01), the ALA Diet decreased vascular cell adhesion molecule-1 (VCAM-1, -15.6% vs. -3.1%, P<0.01) and E-selectin (-14.6% vs. -8.1%, P<0.01) more than the LA Diet.

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Author, Year, Study Design, Class, Rating	Study Description, Duration	Study Population, Demographics	Intervention	Significant Outcomes	Limitations

Hodge AM, English DR et al, 2007 Study Design: Prospective Cohort Study Class: B Rating:		N=3,737 adults. Age: 36 to 72 years. Location: Australia.	Assessed FA intake and Plasma PL-FA and diabetes. Diabetes incidence assessed by self report four years later. Conducted logistic regression: • Excluding (model 1) • Including (model 2). BMI and WHR used to calculate OR for plasma PL and dietary FA.	Positive association between plasma PL and diabetes for: Stearic acid [OR model 1 highest vs. lowest quintile: 4.14 (95% CI: 2.65, 6.49), P≤0.0001]. Total SFA [OR model 1: 0.22 (0.14, 0.36), P≤0.0001] An inverse association for: LA [OR model 1: 3.76 (2.43, 5.81) P≤0.0001]. Dietary LA [OR model 1: 1.77 (1.19, 2.64), P≤0.002].	None.
Jakobsen MU, O'Reilly EJ et al, 2009 Study Design: Meta-analysis or Systematic Review Class: M Rating:	Review of pooled analysis: Proportional Hazards Model.	Pooled data from 11 American and European cohort studies published between 1966 and 1993. Four- to 10-year follow-up. Location: International.	Replacement of SFA intake with MUFA, PUFA and CHO. 5,249 coronary events and 2,155 coronary deaths occurred among 344,696 persons (71% women).	Significant inverse association between substitution of SFA with PUFAs and risk of: • Coronary events (HR: 0.87, 95% CI: 0.77, 0.97) • Coronary deaths (HR: 0.74, 95% CI: 0.61, 0.89). Association between substitution of MUFAs and risk of coronary events (HR: 1.19; 95% CI: 1.00, 1.42), but not risks of coronary deaths. Significant association between substitution of CHO and risk of coronary events (HR: 1.07; 95% CI: 1.01, 1.14) but not risks of coronary deaths. No effect modification by sex or age.	Demographics of US or European populations not described. Type of CHO in the diet not taken into account (i.e., extent of processing, fiber content or glycemic index).
Laaksonen DE, Nyyssonen K et al, 2005 Study Design: Prospective Cohort Study	15-year follow-up.	Initial N=2,682 men who were 42, 48, 54 or 60 years of age at baseline. Final N=1,551. Mean age = 52 years.	Assess the association of dietary fat quantity and quality (LA and ALA) with CVD and overall mortality.	Median follow-up: 14.6 years. 78 men died of CVD; 225 died of any cause. Men with lower dietary	None.

Class: B Rating:		Mean BMI = 26.5±3.4kg/m^2. Location: Finland.		intake of LA and ALA had a higher CVD and overall mortality after adjustment for age and year of examination (P<0.01 to P<0.05). Intake of total fat, SFA, MUFA and cholesterol was not associated with CVD. Men with dietary LA acid intake in the upper third were up to 61% less likely to die of CVD than their counterparts whose intake was in the lower third (RR, 0.39; 95% CI: 0.19 to 0.1, P<0.01). ALA acid was NS associated with CVD mortality. Dietary PUFA intake in the upper third associated with up to 62% ↓ risk of CVD mortality (RR, 0.38; 95% CI: 0.20 to 0.70, P<0.001).	
Liou et al 2007 Study Design: Randomized Crossover Trial Class: A Rating:	Two diets. Four-week period. No washout period.	24 healthy men. Age: 27.9±1.1 years. Attrition: 8%. Location: Canada.	Replaced high LA oils with low in LA oils on plasma n-3 FA, while maintaining constant ALA. 10-week study design: Two-week pre-study phase to avoid fish and seafood. Followed by four weeks of: • ALA at a constant 1% of energy, with LA:ALA ratio of ~4:1 or 10:1 • High LA (10.5±0.53% of energy as LA, 1.1±0.06% as ALA) • Low LA (3.8±0.12% of energy as LA,	Plasma phospholipid-LA higher and EPA lower with intake of high LA than low LA (P<0.001). DHA ↓ over the eight-week period (P<0.001). LA was inversely associated with EPA (R=-0.729, P<0.001), but positively associated with ALA:EPA (R=0.432, P<0.001). LA intake did not influence ALA, arachidonic acid, DPA, DHA, TC, LDL-C; HDL-C. LA intake did not affect CRP, interleukin-6 or platelet aggregation.	Relatively small sample size; only men studied. No washout period.

			1.0±0.05% as ALA). Measured plasma lipids and inflammatory biomarkers.		
Mozaffarian D, Ascherio A et al, 2005 Study Design: Prospective 14-year follow-up study of dietary n-3 and n-6 intake assessed by administration of a self-administered validated FFQ at multiple time points and development of CHD assessed by biennial health history questionnaire. Class: B Rating:	Health Professionals Follow-up Study. 14-year follow-up.	N=45,722 male health professionals. Age: 40 to 75 years. Free of known CVD at baseline. Location: United States.	Investigated the association between intermediate and long-chain n-3 and n-6 PUFA intake on the incidence of CHD. Self-administered FFQ at baseline and every four years to assess dietary intake. Development of CHD assessed by biennial health history questionnaire.	Both long-chain and intermediate-chain n-3 PUFA intakes were associated with ↓ CHD risk, without modification by n-6 PUFA intake. Intermediate-chain n-3 PUFAs were associated with CHD risk, when n-3 PUFA intake was very ↓. In men with n-3 PUFA intake <100mg per day, each 1g per day of intermediate-chain n-3 PUFA intake associated with an ~50% lower risk of non-fatal MI (HR=0.42, 95% CI: 0.23 to 0.75) and total CHD (HR=0.53, 95% CI: 0.34 to 0.83).	None.
Oh K, Hu FB et al, 2005 Study Design: Prospective Cohort Study Class: B Rating:	Nurses' Health Study.	N=78,778 (females, registered nurses). Age: 30 to 55 years in 1976. Average BMI: 24 kg/m^2. Location: United States.	61-item FFQ expanded to 116-items for use in 1984 to 1998. Collected data on dietary intake during the previous year (1980). Follow-up to assess CHD incidence was conducted through June 1, 2000. Endpoint: Non-fatal MI or fatal CHD that occurred after 1980.	1,766 incident CHD cases documented during follow-up (1,241 nonfatal MI; 525 CHD deaths). PUFA intake inversely associated with CHD risk (multivariate RR for the highest vs. lowest quintiles = 0.75, 95% CI: 0.60 to 0.92, P<0.004). TFA intake associated with ↑ risk of CHD (RR=1.33, 95% CI: 1.07 to 1.66, P<0.01). SFA and MUFA not predictors of CHD. Associations of PUFA and TFA were most evident among women <65 years (PUFA: RR=0.66, 95% CI: 0.50 to	None.

				0.85, P<0.002; TFA: RR=1.50, 95% CI: 1.13 to 2.00, P<0.01). PUFA intake and CHD risk was strongest among women with a ≥BMI of 25kg/m^2 (RR=0.63, 95% CI: 0.47 to 0.84, P<0.002).	
St-Onge et al 2007 Study Design: Randomized Crossover Trial Class: A Rating:	Three 25-day feeding periods. Separated by four- or eight-week washout over seven months.	33 subjects (seven male, 26 female). Age: 41.8±1.9 years. Attrition rate: 26%. Location: United States.	Replaced low-fat, high-fat or high-SFA and high-TFA snack foods with high PUFA and low in SFA and TFA snacks. Same base diet except for the types of snacks followed. Low fat: 30.8% of energy from fat, 5.2% of energy from PUFAs. High-PUFA: 36.3% of energy from fat, 9.7% of energy from PUFAs. High-fat: 37.9% of energy from fat, 5.8% of energy from PUFAs. All foods were provided.	All three diets reduced LDL-C and TC concentrations. LDL-C ↓ by 11.8% on low-fat, 12.5% on high-PUFA. Compared with 8.8% on high fat (P=0.03 and P=0.01, respectively). TC ↓ by 0.5% on low-fat ,10.7% on high-PUFA. Compared with: 7.9% on high fat (P=0.03 and P=0.02, respectively).	High attrition rate. Limited power and ability to generalize results. Compliance not clear. Sponsored by Frito Lay.
Thijssen et al 2005 Study Design: Randomized Crossover Trial Class: A Rating:	Three test diets for five weeks. Washout period of at least a week between diets.	N=45 (18 men, 27 women) healthy subjects. BMI: 24.9±2.7kg/m^2. Mean age: 51±10 years (range, 28 to 66 years). Location: Netherlands.	Stearic vs. oleic vs. linoleic acids. Platelet aggregation, coagulation, fibrinolysis and hematological variables. Three test diets consumed in random order over three five-week periods. Test diets: ~35% energy from test fats.	High LA diet: Number of erythrocytes ↓; platelet aggregation favorably prolonged compared to stearic. Stearic acid: ↓ platelet volume compared to LA and OA (P<0.001); no FA effects on coagulation and fibrinolytic variables.	Sponsored by the Dutch Dairy Association.

Thijssen MA and Mensink RP, 2005 Study Design: Randomized Controlled Trial Class: A Rating: 	Three test diets consumed over three five-week periods. Washout period of at least a week between diets.	N=45 (18 men, 27 females) healthy subjects. BMI: 24.9±2.7kg/m^2. Mean age: 51±10 years. Age range: 28 to 66 years. Location: Netherlands.	Compared effects of stearic acid, oleic acid and linoleic acid on serum lipids and lipoproteins. Three test diets consumed in random order over three five-week periods. Test diets: ~35% energy from test fats.	NS diet-induced Δ in serum lipids and lipoproteins were found. Mean serum LDL (mmol per L): • Stearic acid: 3.79+0.9. • Oleic acid: 3.71+0.79. • LA: 3.65+0.91. (P=0.137). Mean serum HDL (mmol per L): • Stearic acid: 1.45+0.43. • Oleic acid: 1.46+0.45. • LA: 1.46+0.44. (P=0.866). LDL, HDL and VLDL particle sizes and lipoprotein subclass distributions did not differ significantly.	Recruitment methods were not described. Sponsored by the Dutch Dairy Association.
Zhao et al 2004 Study Design: Randomized Crossover Trial Class: A Rating: 	Three diets. Six weeks each. Washout period less than three weeks.	N=23 (20 men, three women). Mean age: 49.8±1.6 years. Moderate hypercholesterolemia: Serum TC=5.17 to 6.21mmol per L; LDL-C = 40th to 90th percentile. Body weight (kg) (mean±SEM): All, 86.7+2.8; males, 88.5+2.8; females, 74.9+8.3. BMI (kg/m^2) (mean+SEM): All, 28.1+0.7; men, 28.0+0.7; women: 28.5+2.4. Location: United States	ALA vs. LA vs. Average American Diet (AAD). Two test diets: 35% of energy as fat, 50% as CHO, 15% as PRO and 300mg per day of cholesterol. ALA diet: 17% of energy from PUFA (10.5% LA, 6.5% ALA). LA diet:16.4% of energy from PUFA (12.6% LA, 3.6% ALA). AAD: 8.7% of energy from PUFA (7.7% LA, 0.8% ALA).	Both high-PUFA diets ↓ serum TC, LDL-C and TG similarly (P<0.05). ALA diet significantly ↓ CRP (P<0.01) with greater reduction in intercellular cell adhesion molecule-1, vascular cell adhesion molecule-1 and E-selectin.	Small sample size; mostly of men. AAD not well defined. Sponsor: California Walnut Commission.

Research Design and Implementation Rating Summary

For a summary of the Research Design and Implementation Rating results, click here.

Worksheets

Hodge AM, English DR, O'Dea K, Sinclair AJ, Makrides M, Gibson RA, Giles GG. Plasma phospholipid and dietary fatty acids as predictors of type 2 diabetes: Interpreting the role of linoleic acid. *Am J Clin Nutr.* 2007 Jul; 86 (1): 189-197.

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